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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Appellant(s): Deuel et al.

92-3627
Scott J. Meyer
For Appellant

EXAMINER'S ANSWER

This is in response to appellants' brief on appeal filed on March 3, 1992.

(1) Status of claims

The statement of the status of claims contained in the brief is correct, except appellant misstated that the Director of Group 120 made the decision on the petition filed November 18, 1991. It was the Director of Group 180 that made the decision.

(2) Status of amendments after final

There were no amendments filed after final rejection.

(3) Summary of invention

The summary of the invention contained in the brief is correct.

(4) Issues

The appellants' statement of the issues in the brief is correct.

(5) Grouping of claims

The claims do stand or fall together. The human HBGF-8 protein for which the human HBGF-8 DNA recited in claims 4 and 5, is only 1.8% different in amino acid sequence from the bovine HBGF-8 protein, for which the DNA sequence is recited in claims 6 and 7. This difference is so small to be almost negligible, therefore the DNA sequences are not obvious in view of each other and should be considered together. Furthermore, generic claims 4 and 6 encompass the sequences in claims 5 and 7 and therefore, should be considered together.

(6) Claims appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(7) References of record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

Bohlen, EP 0326075, 2/8/89

Rauvala, EMBO J., 8:2933-2941 (1989)

Maniatis, "Molecular Cloning: A Laboratory Manual," (Cold Spring Harbor Laboratory), New York: 1982, p. 353-361

(8) New prior art

No new prior art is being applied.

(9) Grounds of rejection

Claims 4-7 are rejected under 35 U.S.C. 103 as being unpatentable over Bohlen (EP 0326075) or Rauvala (EMBO J., 1989) et al. in view of Maniatis et al.. Claims 4-7 are drawn to a human and bovine DNA sequence for heparin-binding growth factor. Bohlen and Rauvala both teach purification of an 18 kd heparin-binding protein, and determine N-terminal sequence information (See section 6 of Bohlen and p.2934 of Rauvala). The references do not teach the cloning of the cDNA sequence, however Maniatis et al. teach methods of

determining the cDNA sequence by screening a library with a probe derived from the N-terminal sequence of a protein.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to clone the gene for HBGF, thus achieving the invention as a whole for the expected benefits of determining the full DNA and protein sequences and enabling recombinant production of the protein. The cloning procedures are used in the manner taught by the prior art for the purposes taught by the prior art. One would have been motivated to clone the HGBF gene since the N-terminal sequence of the purified protein had been determined and published. Accordingly, claims 4-7 are prima facie obvious over the prior art, absent sufficient objective factual evidence to the contrary.

(10) New grounds of rejection

There are no new grounds of rejection.

(11) Response to argument

Appellants' initial argument states that claims 4-7 are unobvious over the cited art because that art contains not a single iota of disclosure of any part of the DNA compounds of said claims. Appellants further state that the primary references are completely non-relevant to appellants' DNA claims since they merely teach a protein and are not even concerned with the general field of molecular biology, that the secondary reference is nothing more than state-of-the-art treatise on methods of gene cloning, and that both the structure and properties of the compound must be considered under 35 USC 103. It is maintained that appellants' arguments are unfounded and unconvincing for the following reasons.

It is true that the primary references do not teach any DNA sequences. However, in examining the prior art, one must look at the references as a whole in light of related references and the state of the art at the time of the invention. It is true that nobody had isolated the DNA sequence of HBGF at the time of appellants' filing, however the primary references show that the HBGF protein had been isolated, and purified sufficiently to determine a N-terminal sequence. This is important in relation to appellants' invention because the DNA and the protein, although two different chemical structures and therefore patentably distinct, are related. Proteins that have been purified enough so that sequence structure can be determined are very important to a molecular biologist whose goal is to clone the gene for the protein. This is where the teachings of Maniatis and the state-of-the-art are considered. Maniatis teaches in depth how to use a protein's N-terminal sequence to develop a DNA probe, which is then used to probe a DNA library, and finally purify the gene. This "treatise" was published in 1982, and became such a useful tool to molecular biologists, that by the time of appellants' filing (1990) these procedures were fairly routine. The significant hurdle in this process is purifying the protein, and determining a piece of amino acid sequence. Once this is accomplished, the remaining steps to determine the DNA sequence have become standard and routine in most laboratories. It is the knowledge of the structure and properties of the protein and the DNA that make these procedures possible. The knowledge of the protein's amino acid sequence, coupled with the knowledge in the art in 1990 of how a particular amino acid sequence is derived from a particular DNA sequence, and the properties of each in hybridization assays lead the skilled artisan directly to the cloned gene.

Appellants have stated that the examiner has failed to point out the

homology between the recited DNA sequence in Maniatis and appellants' claimed sequence. Of course there is no homology, since Maniatis does not discuss HBGF or it's amino acid and DNA sequences. Maniatis is cited as a general teaching of routine techniques known in the art, and when read in combination with the primary references, makes obvious the instant claims.

This discussion leads to appellants' second assertion that the rejection under 35 USC 103 should be reversed because it is based on an improper combination of primary and secondary references. It is still maintained that the combination of references is proper and render obvious the instant claims for the following reasons. The examiner agrees with the citations presented in the brief, In re Bergel, and In re Regel. There is a clear motivation for combining these references, and the reasoning lies in the state-of-the-art at the time of appellants' filing. As stated above, proteins that have been purified enough so that sequence structure can be determined are very important to a molecular biologist whose goal is to clone the gene for the protein. Furthermore, there is motivation to clone the gene for a given protein since doing so enables production of large amounts of the protein, determination of particular domains related to specific activities, and generally enhances knowledge of the protein and it's uses. In light of the motivation to clone a gene given part of the protein's amino acid sequence, the reasoning for the combination of references is perfectly clear.

Appellants further argue that the cloning of the HBGF gene is merely obvious to try, which is irrelevant to the Section 103 test of obviousness. However In re O'Farrell (CAFC 7USPQ2d 1673, 1988) states "Finding of obviousness under 35 USC 103 requires only that prior art reveal reasonable expectation of success in producing claimed invention, rather than absolute prediction of such success" and that the application of the impermissible